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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/805,977	03/22/2004	Matthew Oliver Fraser	046562/274660	1508

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EXAMINER

SPIVACK, PHYLLIS G

ART UNIT	PAPER NUMBER
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1614

MAIL DATE	DELIVERY MODE
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09/28/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/805,977

Applicant(s)

FRASER ET AL.

Examiner

Phyllis G. Spivack

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 February 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 67-88 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 67-88 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>1/26/07; 2-16-07; 5-4-07</u> . | 6) <input type="checkbox"/> Other: _____ |

An Amendment filed February 27, 2007 is acknowledged. Claims 67-88 remain under consideration

Applicants' arguments have been fully considered and are persuasive. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. There are no method claims in the instant application.

The abstract of the disclosure is objected to because there are no method claims in the instant application. Correction is required. See MPEP § 608.01(b).

Claims 75-79 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claims, or amend the claims to place the claims in proper dependent form, or rewrite the claims in independent form. Claims 75-79 are directed to intended use of the claimed compositions and thus do not further limit the subject matter of independent claim 67.

Claims 68 and 88 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The recitations in claims 68 and 88, respectively, "in an amount equal to or less than about 5 mg" and "in an amount less than about 2.5 mg" lack clarity. The amount in each claim may be zero.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 67-88 are rejected under 35 U.S.C. 103(a) as being unpatentable over Oberpenning et al., Current Opinion in Urology, in view of Madersbacher et al., BJU International, Ikeda et al., Naunyn-Schmiedeberg's Arch. Pharmacol., and Thor et al., US 2006/0188575.

Oberpenning teaches medical treatment for interstitial cystitis, a chronically progressive, severely debilitating syndrome of the urinary bladder, a lower urinary tract

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disorder, associated with urgency, frequency and pain. See the first paragraph at the top of column one, page 326, where both tolterodine and oxybutynin are recognized in treating overactive bladder and urge symptoms. Further, under **New oral agents**, it is disclosed that the addition of gabapentin to a dosing regimen improved interstitial cystitis functionally and reduced pain. Oberpenning fails to discuss the administration of pregabalin, propiverine or solifenacin, as well as doses for the active agents.

Madersbacher teaches the administration of the antimuscarinic agent propiverine in the treatment of urinary urgency and urge incontinence, symptoms related to detrusor hyperactivity, and further states propiverine is as effective as oxybutynin. See the Abstract. A dosage of 15 mg was given. A dosage of 2.5 mg of oxybutynin was administered.

Ikeda teaches the administration of the antimuscarinic agent solifenacin in the treatment of overactive bladder and also draws comparisons to oxybutynin. A dosage of 0.03 to 1 mg/kg was given. See the Abstract. As required by instant claim 88, Ikeda teaches a dosage range based on body weight that would yield an amount of oxybutynin less than 2.5 mg if the disclosed factor of 0.03 was employed.

Thor teaches equivalence between the $\alpha_2\delta$ subunit calcium channel modulators gabapentin and pregabalin in the treatment of lower urinary tract disorders characterized by overactivity. See page 11, paragraph [0091]. Further, Thor establishes the administration of antimuscarinics as the primary medications used for the treatment of overactive bladder. See page 1, paragraph [0007]. As required by

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instant claims 68 and 69, Thor teaches a wide range of suitable dosage amounts depending on the mode of administration. See pages 21-22, paragraphs [0158] [0160].

Therefore, in view of the combined teachings of the prior art, one skilled in the art of formulation chemistry would have been motivated to prepare a pharmaceutical composition comprising the $\alpha_2\delta$ subunit calcium channel modulators gabapentin and pregabalin with an antimuscarinic agent, such as oxybutynin, tolterodine, propiverine or solifenacin, that are known in the urology art to be effective in the treatment of various lower urinary tract disorders, optionally characterized by urgency, bladder overactivity, frequency, nocturia or incontinence. Such would have been obvious in the absence of evidence to the contrary because both $\alpha_2\delta$ subunit calcium channel modulators, such as gabapentin and pregabalin, and antimuscarinic agents, such as oxybutynin, tolterodine, propiverine or solifenacin, are individually established in the prior art as effective in the treatment of the conditions recited *supra*.

The instant situation is amenable to the type of analysis set forth in *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose. The idea of combining them logically flows from their having been individually taught in the prior art. With respect to the instant claims, one of ordinary skill in the art would have been imbued with at least a reasonable expectation of success by administering the $\alpha_2\delta$ subunit calcium channel modulators gabapentin and pregabalin with an antimuscarinic agent, such as oxybutynin, tolterodine, propiverine or solifenacin, as taught by Oberpenning, Madersbacher, Ikeda, and in

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particular, Thor, which, in addition to Oberpenning, provides motivation to seek the claimed combination formulation for treating various symptoms of lower urinary tract disorders.

An additional rationale for combining references is a clear recognition that mechanisms of action greatly differ between $\alpha_2\delta$ subunit calcium channel modulators and antimuscarinics.

With respect to claimed ratios of claims 72 and 73 of $\alpha_2\delta$ subunit calcium channel modulators to antimuscarinics in the instant compositions, it is not inventive to discover the optimum or workable ranges by routine experimentation when general conditions of a claim are disclosed in the prior art. See *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233,235 (CCPA 1955) and MPEP 2144.05(II). These determinations of the optimum ratios to employ with the presently claimed active agents would be within the purview of one of ordinary skill in the art. Such determination would have been made in accordance with a variety of factors. These would have included such factors as the age, weight, sex, diet and medical condition of the patient, severity of the disease, the route of administration, pharmacological considerations, such as the activity, efficacy, pharmacokinetics and toxicology profiles of the particular compound employed, whether a drug delivery system is utilized and whether the compound is administered a part of a drug combination. Thus, in the absence of evidence to the contrary, the currently claimed specific ratios are not seen to be inconsistent with those that would have been determined by the skilled artisan.

No claim is allowed.

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Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Phyllis G. Spivack whose telephone number is 571-272-0585. The Examiner can normally be reached from 10:30 to 7 PM.

If attempts to reach the Examiner by telephone are unsuccessful after one business day, the Examiner's supervisor, Ardin Marschel, can be reached 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

September 25, 2007



Phyllis Spivack

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**PHYLLIS SPIVACK
PRIMARY EXAMINER**